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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/039,119	01/04/2002	Daniel R. Twardzik	STEM1110-4	1736

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EXAMINER	
GUCKER, STEPHEN	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/039,119	TWARDZIK ET AL.	
	Examiner	Art Unit	
	Stephen Gucker	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 73-78 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 73-78 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 1/4/02, 11/26/02.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claim 78 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. A method for organ repair comprising stimulation of a population of CD34+ cells is not supported by the specification on page 51, lines 13-17, as indicated by Applicant. This is a new matter rejection.

3. Claims 73-78 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for TGF-α polypeptide set forth in SEQ ID NO:1 (also shown in Figure 1) or the fragment known as Loop C (residues 33-50 of SEQ ID NO:1), does not reasonably provide enablement for any other TGF mimetic or TGF related polypeptide or other functional fragment thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The evidence of record describes biologically active TGF polypeptide amino acids 1-50 (SEQ ID NO:1) and a single fragment, amino acids 33-50 referred to as Loop C, formed by the positions of the disulfide bonds produced by the cysteines in the amino acid

chain (see Figure 1). The specification teaches that TGF Loop peptide C, amino acids 33-50, had significant TGF activity as determined by cell proliferation assay, while Loop A (amino acids 1-21) and Loop B (amino acids 16-32) did not have significant biological activity (lines 19-21, page 5). The specification does not provide an adequate written description, examples, or guidance by which the enablement of the genus of variant TGF mimetics is achieved because the disclosure teaches that the whole TGF polypeptide and a single fragment possessed biological activity while other fragments did not. The specification fails to disclose what the common structural feature of TGF-α polypeptide is that bestows upon it its desired and recited biological properties, other than its N-terminal fragment, amino acids 33-50 of SEQ ID NO:1. Because of the high unpredictability in the peptide arts, a biologically active peptide with one identified active fragment cannot adequately describe or enable the scope of the genus claimed which encompasses additions, substitutions, and deletions to the single species of active fragment because such variations in the peptide structure would require undue experimentation (Rudinger, page 6, or "painstaking experimental study" as noted by Rudinger) because the effect of any amino acid substitution, addition, or deletion on a polypeptide's desired and claimed function cannot be predicted *a priori*. Even when a partial sequence to a biologically active peptide is rigidly defined without resorting to variable substitutions, deletions, and additions, it has been held that claims to a genus of peptides with a partial structure and a specific biological activity were not enabled (*In re Fisher, 166 USPQ 19*). As in *Fisher*, the instant disclosure offers only assertions that the genus of peptides taught possess the desired biological property, while Applicant's

own teachings and the prior art demonstrate that only the full length peptide and amino acids 33-50 of the full length peptide possess biological activity. The CCPA noted in *Fisher* in regards to the scope of the genus of ACTH peptides claimed that:

> "...appellant's conclusion that the 25th to 39th acids in the chain are unnecessary, it is one thing to make such a statement when persons skilled in the art are able to make or obtain ACTH having other than 39 amino acids; it is quite another thing when they are not able to do so."(22)

The evidence of record describes biologically active TGF-α polypeptide amino acids 1-50 (SEQ ID NO:1) and a single fragment, amino acids 33-50 referred to as Loop C, formed by the positions of the disulfide bonds produced by the cysteines in the amino acid chain (see Figure 1). There is insufficient basis to demonstrate that the claimed genus of methods using many variant peptides is in fact enabled by a single species of active fragment given the high degree of unpredictability in the peptide arts as taught in the prior art exemplified by Rudinger.

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 73-75 and 78 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 7-8, and 10

of U.S. Patent No. 6,486,122 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims recite a method of using a composition identical to both the patent and the instant application, human TGF-α polypeptide (SEQ ID NO:1). The preambles of both sets of claims do not provide any patentable distinction between the two sets of claims because treating weight loss or inducing weight gain (the patent) or expanding the population of CD34 positive cells in a human subject (the application), are both treatment methods for symptoms of the same diseases, AIDS or cancer.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 73-75 and 78 are rejected under 35 U.S.C. 102(b) as being anticipated by Todaro (US 5,240,912). Todaro teaches TGF-α polypeptides (column 4, lines 18-44) which meet the limitations of the products used in the instant claims. Additionally, Todaro describes the use of the TGF polypeptides administered subcutaneously, intramuscularly, and intraperitoneally (column 15, lines 32-36). The therapeutic methods taught by Todaro inherently possess the property of expanding the population of CD34

positive cells in a human subject because the products taught in the prior art and the instant Application are identical and the instant Application does not disclose any special manner or mode of administration that is novel or different over the prior art administration of the identical prior art product.

8. Claims 73-75 and 78 are rejected under 35 U.S.C. 102(b) as being anticipated by Ogawa et al. (JP 410158188A, "Ogawa JP"). Ogawa JP discloses methods using TGF-α polypeptide in combination with SCF systemically and parenterally to treat corneal disorders (column 1, lines 1-13; column 3, lines 37-50; and column 5, lines 8-11) which would inherently meet the limitation of expanding the population of CD34 positive cells in a human subject because the products taught in the prior art and the instant Application are identical and the instant Application does not disclose any special manner or mode of administration that is novel or different over the prior art administration of the identical prior art product.

9. Claims 73-75 and 78 are rejected under 35 U.S.C. 102(b) as being anticipated by Amagase et al. (US 4,863,902, "Amagase"). Amagase discloses a method of using human TGF-α during cytotoxic therapy (column 9, lines 29-46; column 29, line 38 to column 30, line 22; column 35, lines 3-52; and claims 53-55 and 59) which would inherently meet the limitation of expanding the population of CD34 positive cells in a human subject because the products taught in the prior art and the instant Application are identical and the instant Application does not disclose any special manner or mode of administration that is novel or different over the prior art administration of the identical prior art product.

10. Claims 73-75 and 78 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Zhang (US 5,814,308). Zhang discloses methods using TGF-α polypeptide and other agents in patients undergoing cytotoxic chemotherapy and/or immune suppression which meet the limitation steps of the instant claims (column 1, lines 64-65; column 2, lines 17-29; column 7, lines 15-49) and would inherently meet the limitation of expanding the population of CD34 positive cells in a human subject because the products taught in the prior art and the instant Application are identical and the instant Application does not disclose any special manner or mode of administration that is novel or different over the prior art administration of the identical prior art product.

11. Claims 73-75 and 78 are rejected under 35 U.S.C. 102(e) as being anticipated by Ogawa et al. (US 5,942,487, "Ogawa US"). Ogawa US discloses methods using TGF-α polypeptide in combination with SCF systemically and parenterally to treat corneal disorders (abstract; column 3, lines 25-50; and column 4, lines 44-54) which would inherently meet the limitation of expanding the population of CD34 positive cells in a human subject because the products taught in the prior art and the instant Application are identical and the instant Application does not disclose any special manner or mode of administration that is novel or different over the prior art administration of the identical prior art product.

12. No claim is allowed.

13. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technical Center 1600 general number which is (571) 272-1600.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is (571) 272-0883. The examiner can normally be reached on Monday to Friday from 0930 to 1800. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (571) 272-0887. The fax phone number for this Group is currently (703) 872-9306.

Gary L. Kunz

GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Stephen Gucker

May 17, 2004